IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent

In re patent application of: MONTEIL ET AL.

Serial No.: Unassigned — Examiner: Unassigned

Filed: On even date herewith — Art Unit: Unassigned

For: PROCESS FOR SYNTHESIZING ... — Dckt No.: P07428US00/BAS

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents

Washington, D.C. 20231

SIR:

Prior to examination, please amend the above-identified application as follows:

IN THE CLAIMS

A clean version of all pending claims is provided herewith in **Attachment A**. It will be noted that claims 3, 6-10 and 13-16 have been amended relative to the previously provided version as shown by the marked up version thereof in **Attachment B** provided herewith.

REMARKS

The present amendment is made to eliminate multiple dependent claims and thus eliminate the requirement for a multiple claim fee.

Respectfully submitted,

Date: November 9, 2001

By: Douglas E. Jackson
Registration No.: 28,518

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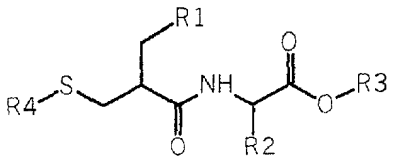
ATTACHMENT A

Clean Replacement/New Claims (entire set of pending claims)

Following herewith is a clean copy of the entire set of pending claims.

1. Process for preparing a compound of formula (I):



(I)

wherein :

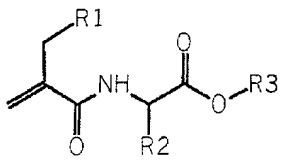
- R1 represents: - a phenyl group; or
  - a 3,4-methylenedioxyphenyl group
- R2 represents a hydrogen atom or a lower alkyl group;
- R3 represents a hydrogen atom, a lower alkyl group or a lower phenylalkylene group; and
- R4 represents a linear or branched aliphatic acyl radical or an aromatic acyl radical,

said process comprising a step (B) which consists in performing a Michael addition of a thioacid of formula (IV):

R4SH (IV)

wherein R4 has the same meaning as in formula (I),

with an α-substituted acrylamide derivative of formula (V):

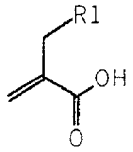


(V)

wherein R1, R2 and R3 have the same meaning as in formula (I).

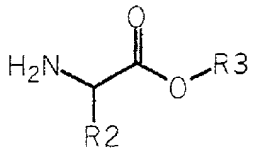
2. Process according to claim 1, wherein the group R4 represents an acetyl radical CH_3-CO-, a benzoyl radical C_6H_5-CO- or a pivaloyl radical $CH_3)_3$-CO-.

3. (amended) Process according to claim 1, wherein said α-substituted acrylamide derivative of formula (V) is obtained from a step (A), prior to step (B), comprising a step consisting in performing the coupling of an acrylic acid of formula (VI):



(VI)

wherein R1 has the same meaning as in formula (I),
with an amino ester of formula (VIII):

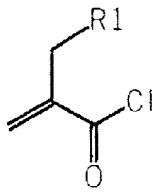


(VIII)

wherein R2 and R3 have the have the same meaning as in formula (I).

4. Process according to claim 3, wherein said step (A) comprises the successive steps consisting in:

(A1) reacting said α-substituted acrylic acid of formula (VI) with an chloro acid so as to obtain an acid chloride of formula (VII):



(VII)

wherein R1 has the same meaning as in formula (I);

and

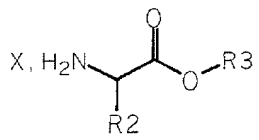
A2) reacting the acid chloride of formula (VII) thus obtained with said amino ester of formula (VIII), in the presence of a base, so as to achieve the coupling.

5. Process according to claim 4, wherein the chloro acid used in step (A1) is chosen from $SOCl_2$, ClCO-COCl, PCl_3 and PCl_5.

6. (amended) Process according to claim 4, wherein the acid chloride of formula (VII) obtained from step (A1) is subjected to a distillation step before being used in step (A2).

7. (amended) Process according to claim 4, wherein the base used in step (A2) is an organic amine.

8. (amended) Process according to claim 1, wherein the amino ester used in step (A2) is introduced in the form of a salt of formula (VIIIa):



(VIIIa)

wherein R2 and R3 have the have the same meaning as in formula (I); and wherein X is chosen from HCl, CH_3SO_3H and 4-methylphenyl-SO_3H.

9. (amended) Process according to claim 4, wherein step (A2) is carried out in the presence of an organic solvent chosen from toluene, dichloromethane, 1,2-dichloroethane, chloroform, N,N-dimethylformamide, 1,4-dioxane, N-methylpyrrolidone, N,N-dimethylacetamide, butyl acetate, ethyl acetate, isobutyl acetate, isopropyl acetate, methyl acetate, propyl acetate and tetrahydrofuran.

10. (amended) Process according to claim 1, wherein compound (V) used in step (B) is a chiral compound wherein R2 denotes a lower alkyl group, said compound (V) being used at least predominantly in its S configuration or at least predominantly in its R configuration.

11. Process according to claim 10, wherein compound (V) is used in its ptically pure S form.

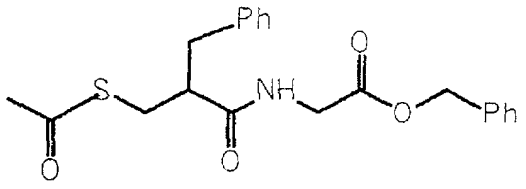
12. Process according to claim 11, wherein compound (V) is prepared by a condensation reaction of an acrylic acid of formula (VI) with an amino ester of formula (VIII) derived from a natural amino acid.

13. (amended) Process according to claim 10, wherein chirality inducers are used in step (B).

14. (amended) Process according to claim 10, which further comprises,

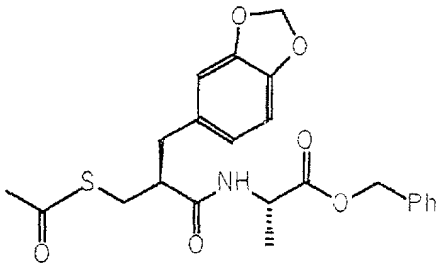
after step (B), a subsequent step (C) of separation of the diastereoisomers obtained in step (B).

15. (amended) Process according to claim 1, wherein said obtained compound of formula (I) is benzyl N-(RS)-[2-acetylthiomethyl-1-oxo-3-phenylpropyl]glycinate of formula (II):



(II)

16. (amended) Process according to claim 1, wherein said obtained compound of formula (I) is benzyl N-(S)-[2-acetylthiomethyl-1-oxo-3-(3,4-methylenedioxyphenyl)propyl]-(S)-alaninate of formula (III):



(III)

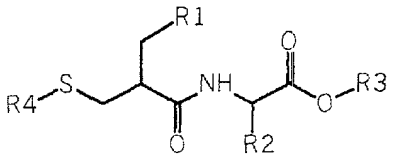
ATTACHMENT B

Marked Up Replacement Claims

Following herewith is a marked up copy of each rewritten claim together with all other pending claims.

Following herewith is a marked up copy of each rewritten claim.

1. Process for preparing a compound of formula (I):



(I)

wherein :

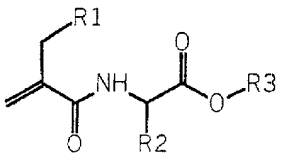
- R1 represents: - a phenyl group; or
  - a 3,4-methylenedioxyphenyl group
- R2 represents a hydrogen atom or a lower alkyl group;
- R3 represents a hydrogen atom, a lower alkyl group or a lower phenylalkylene group; and
- R4 represents a linear or branched aliphatic acyl radical or an aromatic acyl radical,

said process comprising a step (B) which consists in performing a Michael addition of a thioacid of formula (IV):

R4SH (IV)

wherein R4 has the same meaning as in formula (I),

with an α-substituted acrylamide derivative of formula (V):

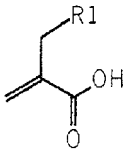


(V)

wherein R1, R2 and R3 have the same meaning as in formula (I).

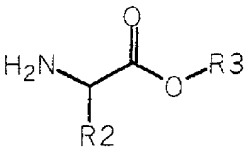
2. Process according to Claim 1, wherein the group R4 represents an acetyl radical CH_3-CO-, a benzoyl radical C_6H_5-CO- or a pivaloyl radical $CH_3)_3$-CO-.

3. (amended) Process according to Claim 1 ~~or according to Claim 2~~, wherein said α-substituted acrylamide derivative of formula (V) is obtained from a step (A), prior to step (B), comprising a step consisting in performing the coupling of an acrylic acid of formula (VI):



(VI)

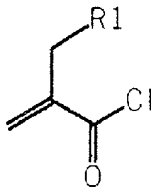
wherein R1 has the same meaning as in formula (I),
with an amino ester of formula (VIII):



(VIII)

wherein R2 and R3 have the have the same meaning as in formula (I).

4. Process according to Claim 3, wherein said step (A) comprises the successive steps consisting in:
(A1) reacting said α-substituted acrylic acid of formula (VI) with an chloro acid so as to obtain an acid chloride of formula (VII):



(VII)

wherein R1 has the same meaning as in formula (I);

and

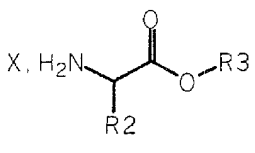
A2) reacting the acid chloride of formula (VII) thus obtained with said amino ester of formula (VIII), in the presence of a base, so as to achieve the coupling.

5. Process according to Claim 4, wherein the chloro acid used in step (A1) is chosen from $SOCl_2$, ClCO-COCl, PCl_3 and PCl_5.

6. (amended) Process according to Claim ~~4 or Claim 5~~, wherein the acid chloride of formula (VII) obtained from step (A1) is subjected to a distillation step before being used in step (A2).

7. (amended) Process according to~~ any one of Claims 4 to 6~~claim 4, wherein the base used in step (A2) is an organic amine.

8. (amended) Process according to~~ any one of Claims 4 to 7~~claim 1, wherein the amino ester used in step (A2) is introduced in the form of a salt of formula (VIIIa):



(VIIIa)

wherein R2 and R3 have the have the same meaning as in formula (I); and wherein X is chosen from HCl, CH_3SO_3H and 4-methylphenyl-SO_3H.

9. (amended) Process according to ~~any one of Claims 4 to 8~~claim 4, wherein step (A2) is carried out in the presence of an organic solvent chosen from toluene, dichloromethane, 1,2-dichloroethane, chloroform, N,N-dimethylformamide, 1,4-dioxane, N-methylpyrrolidone, N,N-dimethylacetamide, butyl acetate, ethyl acetate, isobutyl acetate, isopropyl acetate, methyl acetate, propyl acetate and tetrahydrofuran.

10. (amended) Process according to ~~any one of Claims 1 to 9~~claim 1, wherein compound (V) used in step (B) is a chiral compound wherein R2 denotes a lower alkyl group, said compound (V) being used at least predominantly in its S configuration or at least predominantly in its R configuration.

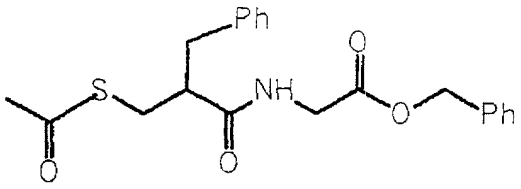
11. Process according to Claim 10, wherein compound (V) is used in its optically pure S form.

12. Process according to Claim 11, wherein compound (V) is prepared by a condensation reaction of an acrylic acid of formula (VI) with an amino ester of formula (VIII) derived from a natural amino acid.

13. (amended) Process according to ~~any one of Claims 10 to 12~~claim 10, wherein chirality inducers are used in step (B).

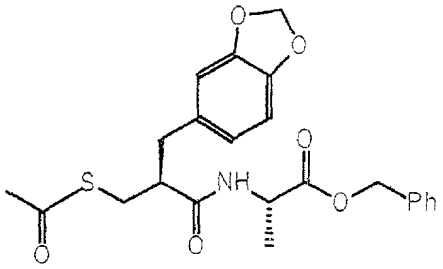
14. (amended) Process according to ~~any one of Claims 10 to 12~~claim 10, which further comprises, after step (B), a subsequent step (C) of separation of the diastereoisomers obtained in step (B).

15. (amended) Process according to ~~any one of Claims 1 to 9~~claim 1, wherein said obtained compound of formula (I) is benzyl N-(RS)-[2-acetylthiomethyl-1-oxo-3-phenylpropyl]glycinate of formula (II):



(II)

16. (amended) Process according to ~~any one of Claims 1 to 14~~claim 1, wherein said obtained compound of formula (I) is benzyl N-(S)-[2-acetylthiomethyl-1-oxo-3-(3,4-methylenedioxyphenyl)propyl]-(S)-alaninate of formula (III):



(III)